

CLAIMS

What is claimed is:

1. An altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into an immunogenic composition or vaccine and
5 administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV.
2. An altered G protein or polypeptide according to Claim 1, wherein the enhanced disease is atypical pulmonary inflammation.
3. An altered G protein or polypeptide according to Claim 2, wherein the atypical
10 pulmonary inflammation is pulmonary eosinophilia.
4. An altered G protein or polypeptide according to Claim 1, wherein the alteration is in the region from amino acid 159 to amino acid 198.
5. An altered G protein or polypeptide according to Claim 4, wherein the alteration
15 is in one or more regions selected from the group consisting of the region from amino acid 159 to amino acid 174, the region from amino acid 171 to amino acid 187, the region from amino acid 176 to amino acid 190, and the region from amino acid 184 to amino acid 198.
6. An altered G protein or polypeptide according to Claim 5, wherein the alteration is in the region from amino acid 184 to amino acid 198.

7. An altered G protein or polypeptide according to Claim 1, wherein the alteration results in inhibition of priming for IL-5 secretion by the altered G protein or polypeptide relative to wild type G protein.
8. An altered G protein or polypeptide according to Claim 1, wherein the alteration results in enhancement of priming for IFN- γ secretion by the altered G protein or polypeptide relative to wild type G protein.
9. A nucleic acid molecule encoding an altered G protein or polypeptide of RSV, wherein said altered G protein or polypeptide retains immunogenicity and, when incorporated into an immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV.
10. A nucleic acid molecule according to Claim 9, wherein the alteration is in the region of the nucleic acid molecule encoding the region from amino acid 159 to amino acid 198.
11. A nucleic acid molecule according to Claim 10, wherein the alteration is in the region of the nucleic acid molecule encoding one or more regions selected from the group consisting of the region from amino acid 159 to amino acid 174, the region from amino acid 171 to amino acid 187, the region from amino acid 176 to amino acid 190, and the region from amino acid 184 to amino acid 198.
12. A nucleic acid molecule according to Claim 11, wherein the alteration is in the region from amino acid 184 to amino acid 198.
13. A nucleic acid construct comprising a nucleic acid molecule according to Claim 9 operably linked to a regulatory sequence.

14. A chimeric nucleic acid construct comprising:
 - a) a nucleic acid molecule encoding an altered G protein or polypeptide of RSV, wherein said altered G protein or polypeptide retains immunogenicity and, when incorporated into an immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV;
 - b) a nucleic acid molecule encoding all or an immunogenic portion of F protein of RSV; and
 - c) a regulatory sequence operably linked to both (a) and (b).
15. A recombinant host cell comprising a nucleic acid construct according to Claim 13.
16. A recombinant host cell comprising a nucleic acid construct according to Claim 14.
17. A method of producing an altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into an immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV, comprising maintaining a recombinant host cell according to Claim 15 under conditions suitable for expression of the altered G protein or polypeptide.
18. A method of producing a chimeric polypeptide comprising an altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into an immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV, and all or an immunogenic portion of F protein of RSV,

comprising maintaining a recombinant host cell according to Claim 16 under conditions suitable for expression of the encoded chimeric protein.

19. An immunogenic composition comprising a physiologically acceptable medium and an altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into an immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV.
20. An immunogenic composition according to Claim 19, wherein the immunogenic composition results in inhibition of priming for IL-5 secretion relative to an immunogenic composition comprising wild type G protein.
21. An immunogenic composition according to Claim 19, wherein the immunogenic composition results in enhancement of priming for IFN- γ secretion relative to an immunogenic composition comprising wild type G protein.
22. An immunogenic composition according to Claim 20, wherein the alteration is in the region from amino acid 159 to amino acid 198.
23. An immunogenic composition according to Claim 22, wherein the alteration is in one or more regions selected from the group consisting of the region from amino acid 159 to amino acid 174, the region from amino acid 171 to amino acid 187, the region from amino acid 176 to amino acid 190, and the region from amino acid 184 to amino acid 198.
24. An immunogenic composition comprising a physiologically acceptable medium, all or a portion of F protein of RSV and an altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into an

immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV.

25. An immunogenic composition according to Claim 24, wherein the immunogenic composition results in inhibition of priming for IL-5 secretion relative to wild-type G protein.
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26. An immunogenic composition according to Claim 24, wherein the immunogenic composition results in enhancement of priming for IFN- γ secretion relative to wild-type G protein.
27. An immunogenic composition according to Claim 24, wherein the alteration is
10 in the region from amino acid 159 to amino acid 198.
28. An immunogenic composition according to Claim 27, wherein the alteration is in one or more regions selected from the group consisting of the region from amino acid 159 to amino acid 174, the region from amino acid 171 to amino acid 187, the region from amino acid 176 to amino acid 190, and the region from
15 amino acid 184 to amino acid 198.
29. An immunogenic composition according to Claim 24, wherein the alteration is in the region having the amino acid sequence alanine-isoleucine-cysteine-lysine-arginine-isoleucine-proline-asparagine-lysine-lysine-proline-glycine-lysine-lysine-threonine or biological equivalents thereof.
- 20 30. A vaccine composition comprising an immunologically effective amount of altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into a vaccine and administered to a vertebrate.

provides protection without inducing enhanced disease upon subsequent infection of the vertebrate with RSV.

31. A vaccine composition according to Claim 30, wherein the alteration is in the region from amino acid 159 to amino acid 198.
- 5 32. A vaccine composition according to Claim 31, wherein the alteration is in one or more regions selected from the group consisting of the region from amino acid 159 to amino acid 174, the region from amino acid 171 to amino acid 187, the region from amino acid 176 to amino acid 190, and the region from amino acid 184 to amino acid 198.
- 10 33. A vaccine composition according to Claim 32, wherein the alteration is in the region from amino acid 184 to amino acid 198.
34. A vaccine composition comprising an immunologically effective amount of all or a portion of F protein of RSV, and an immunologically effective amount of altered G protein or polypeptide of RSV which retains immunogenicity and
15 which, when incorporated into a vaccine and administered to a vertebrate, provides protection without inducing enhanced disease upon subsequent infection of the vertebrate with RSV.
35. A vaccine composition according to Claim 34, wherein the alteration is in the region from amino acid 159 to amino acid 198.
- 20 36. A vaccine composition according to Claim 35, wherein the alteration is in one or more regions selected from the group consisting of the region from amino acid 159 to amino acid 174, the region from amino acid 171 to amino acid 187, the

region from amino acid 176 to amino acid 190, and the region from amino acid 184 to amino acid 198.

37. A vaccine composition according to Claim 36, wherein the alteration is in the region from amino acid 184 to amino acid 198.
- 5 38. A vaccine composition according to Claim 32, further comprising an adjuvant.
39. A vaccine composition according to Claim 35, further comprising an adjuvant.
40. Use of the altered G protein or polypeptide according to Claim 1 for the manufacture of a medicament, such as a vaccine.
41. A vaccine comprising a physiologically acceptable vehicle and an effective
10 amount of a nucleic acid molecule encoding an altered G protein or polypeptide of RSV, where said altered G protein or polypeptide retains immunogenicity and, when incorporated into a vaccine and administered to a vertebrate, provides protection without inducing enhanced disease upon subsequent infection of the vertebrate with RSV.
- 15 42. A vaccine according to Claim 41, further comprising a transfection-facilitating agent.
43. A method of inducing an immune response in a vertebrate, comprising administering to said vertebrate an amount of DNA encoding an altered RSV G protein or polypeptide effective to induce an immune response, and a
20 transfection-facilitating agent, where said altered G protein or polypeptide retains immunogenicity and, when incorporated into a vaccine and administered

to a vertebrate, provides protection without inducing enhanced disease upon subsequent infection of the vertebrate with RSV.

44. A method of inhibiting induction of enhanced disease after vaccination and subsequent infection of a vertebrate with RSV, comprising administering an altered RSV G protein or polypeptide, where said altered G protein or polypeptide retains immunogenicity and, when incorporated into a vaccine and administered to a vertebrate, provides protection without inducing enhanced disease upon subsequent infection of the vertebrate with RSV.
45. A method of immunizing a vertebrate against RSV, comprising administering to the vertebrate a composition comprising an immunologically effective amount of altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into an immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV.
46. A method according to Claim 45, wherein the composition further comprises an immunologically effective amount of all or a portion of RSV F protein.
47. A method according to Claim 45, wherein the vertebrate is an RSV seronegative human.
48. A method of immunizing a vertebrate against RSV, comprising administering to the vertebrate a composition comprising an immunologically effective amount of a nucleic acid molecule encoding an altered G protein or polypeptide of RSV, where said altered G protein or polypeptide retains immunogenicity and, when incorporated into an immunogenic composition or vaccine and administered to a

vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV.

49. A method according to Claim 48, wherein the composition further comprises an immunologically effective amount of a nucleic acid molecule encoding all or a portion of RSV F protein.
50. A method according to Claim 48, wherein the vertebrate is an RSV seronegative human.
51. A vaccine composition comprising an immunologically effective amount of a live attenuated pathogen which has inserted within it as a heterologous nucleic acid segment a nucleic acid sequence encoding an altered G protein or polypeptide of RSV, such that upon administration to the vertebrate, the altered G protein or polypeptide is expressed and is immunogenic, but does not induce enhanced disease upon subsequent infection of the vertebrate with RSV.
52. A vaccine composition according to Claim 51, wherein the live attenuated pathogen is an attenuated bacterium.
53. A vaccine composition according to Claim 52, wherein the live attenuated bacterium is Salmonella.
54. A vaccine composition according to Claim 51, wherein the live attenuated pathogen is an attenuated virus.
55. A vaccine composition according to Claim 54, wherein the live attenuated virus is an attenuated Venezuelan Equine Encephalitis virus.

56. A method of immunizing a vertebrate against RSV, comprising administering to the vertebrate a composition comprising an immunologically effective amount of a live attenuated pathogen which has inserted within it as a heterologous nucleic acid segment a nucleic acid sequence encoding an altered G protein or polypeptide of RSV, such that upon administration to the vertebrate, the altered G protein or polypeptide is expressed and is immunogenic, but does not induce enhanced disease upon subsequent infection of the vertebrate with RSV:
57. A method according to Claim 56, wherein the live attenuated pathogen is an attenuated bacterium.
58. A method according to Claim 57, wherein the live attenuated bacterium is Salmonella.
59. A method according to Claim 56, wherein the live attenuated pathogen is an attenuated virus.
60. A method according to Claim 59, wherein the live attenuated virus is an attenuated Venezuelan Equine Encephalitis virus.
61. An altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into an immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV, said protein or polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33 and SEQ ID NO: 37.
62. An immunogenic composition comprising a physiologically acceptable medium and an altered G protein or polypeptide of RSV which retains immunogenicity

and which, when incorporated into an immunogenic composition or vaccine and administered to a vertebrate, does not induce enhanced disease upon subsequent infection of the vertebrate with RSV, said protein or polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33 and SEQ ID NO: 37.

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63. A vaccine composition comprising an immunologically effective amount of altered G protein or polypeptide of RSV which retains immunogenicity and which, when incorporated into a vaccine and administered to a vertebrate, provides protection without inducing enhanced disease upon subsequent infection of the vertebrate with RSV, said protein or polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33 and SEQ ID NO: 37.

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